

AMENDMENTS

In the specification:

On page 11 at line 32, following "in Enzymology 65," please replace "56--580" with "560-580"

In the claims:

Please cancel claims 1 and 31-72, without prejudice or disclaimer.

Please enter new claims 73-117 as follows:

73. A primer tagged with a chromophore or fluorophore, said chromophore or fluorophore attached so as to allow chain extension by a polymerase.

74. The primer of claim 73, wherein the chromophore or fluorophore is bound to the primer through an amine linkage.

75. The primer of claim 73, wherein the tagged primer has been base-paired to a template.

76. The primer of claim 75, wherein the tagged primer which has been base-paired to a template has been extended by a polymerase.

77. The extended primer of claim 76, wherein the tagged, extended primer has been separated from the template.

Diagonucleotide *Diagonucleotide*
78. A set of primers comprising one or more primers tagged with a chromophore or fluorophore, said chromophore or fluorophore attached so as to allow chain extension by a polymerase.

79. The set of primers of claim 78, wherein the set comprises two or more tagged primers which are distinguishable by the spectral characteristics of the tags.

80. The set of primers of claim 78, wherein the chromophore or fluorophore is bound to the primer through an amine linkage.

Sub E2
81. The set of primers of claim 78, wherein each tagged primer has been base-paired to a template.

Sub E2
82. The set of primers of claim 81, wherein each tagged primer which has been base-paired to a template has been extended by a polymerase.

83. The extended primers of claim 82, wherein the tagged, extended primers have been separated from the template.

Oligonucleotide

84. A set of reagents comprising primers tagged with one or more chromophores or fluorophores, said chromophores or fluorophores attached so as to allow chain extension by a polymerase.

85. The set of reagents of claim 84, wherein the chromophores or fluorophores are bound to the primer through an amine linkage.

86. The set of reagents of claim 84, wherein one or more of the primers are tagged with a chromophore or fluorophore.

87. The set of reagents of claim 84, wherein the set comprises two or more tagged primers and wherein the tagged primers are distinguishable by their spectral characteristics.

88. The set of reagents of claim 84, further comprising a polymerase.

Oligonucleotide
89. An oligonucleotide comprising a primer tagged with a chromophore or fluorophore, said chromophore or fluorophore attached so as to allow chain extension by a polymerase.

90. The oligonucleotide of claim 89, wherein the chromophore or fluorophore is bound to the primer through an amine linkage.

~~91. The oligonucleotide of claim 89, wherein the primer is tagged at its 5' end or in the vicinity thereof.~~

Sub E4
92. The oligonucleotide of claim 89, wherein the tagged primer has been hybridized to a template and extended in length.

93. The oligonucleotide of claim 92, wherein the chromophore or fluorophore is bound to the primer through an amine linkage.

94. The oligonucleotide of claim 92, wherein the primer is tagged at its 5' end or in the vicinity thereof.

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95. The oligonucleotide of claim 92, wherein the oligonucleotide has been separated from the template.

96. The oligonucleotide of claim 95, wherein the chromophore or fluorophore is bound to the primer through an amine linkage.

97. The oligonucleotide of claim 95, wherein the primer is tagged at its 5' end or in the vicinity thereof.

Sub F6
98. An oligonucleotide comprising a first portion tagged with a chromophore or fluorophore so as to allow chain extension, wherein said first tagged portion has been hybridized to a template; and said first tagged portion has been extended so as to create a second portion contiguous with the first.

99. The oligonucleotide of claim 98, wherein the chromophore or fluorophore is bound to the first portion through an amine linkage.

100. The oligonucleotide of claim 98, wherein the first portion is tagged at its 5' end or in the vicinity thereof.

Sub C1
101. A method for preparing a tagged oligonucleotide comprising the steps of:
hybridizing an oligonucleotide fragment tagged with a chromophore or fluorophore to a sequence which is complementary to the oligonucleotide fragment; and
extending the tagged oligonucleotide fragment.

102. The method of claim 101, wherein the chromophore or fluorophore is bound to the oligonucleotide fragment through an amine linkage.

103. The method of claim 101, wherein the oligonucleotide fragment is tagged at its 5' end or in the vicinity thereof.

104. The method of claim 101, wherein the tagged oligonucleotide fragment is extendible by a polymerase.

105. The method of claim 101, further comprising separating the tagged, extended oligonucleotide from the complementary sequence.

106. The method of claim 105, wherein the chromophore or fluorophore is bound to the oligonucleotide fragment through an amine linkage.

107. The method of claim 105, wherein the oligonucleotide fragment is tagged at its 5' end or in the vicinity thereof.

108. The separated oligonucleotide of claim 105.

109. The method of claim 101, wherein the method includes a chain termination DNA sequencing reaction.


C 110. The ^{primer}method of claim 109, wherein, in the performance of a set of one or more chain termination DNA sequencing reactions, the tagged oligonucleotides comprising one of the sets are distinguishable from the tagged oligonucleotides comprising the other sets.

sub
C 111. The ^{primer}method of claim 110, wherein the ^{primer}method includes all four chain termination DNA sequencing reactions, and the tagged oligonucleotides comprising each of the sets are distinguishable by their spectral characteristics from the tagged oligonucleotides comprising each of the other sets.

112. Apparatus for detecting a plurality of aliquots of oligonucleotide fragments, at least two of said aliquots tagged with chromophores or fluorophores, said at least two aliquots being distinguishable by the spectral characteristics of the chromophores or fluorophores, comprising:
a zone for containing an electrophoretic medium for separating said oligonucleotide fragments;
electrodes coupled to said zone for providing an electromotive force across said zone;
a laser for irradiating at least a portion of said zone; and
a detector for monitoring and distinguishing said oligonucleotide fragments, upon separation in said medium, by the spectral characteristics of the chromophores or fluorophores used to tag said oligonucleotide fragments.

113. The apparatus of claim 112 wherein said detector is capable of distinguishing said fragments which differ by as little as a single base.

114. The apparatus of claim 112, wherein said detector comprises a lens system located to gather light emitted from said oligonucleotide fragments.

 115. The apparatus of claim 114, wherein said detector further comprises an optical filter located to receive light from said lens system, said optical filter capable of distinguishing the spectral characteristics of the light gathered by said lens system.

116. The apparatus of claim 115, wherein said detector further comprises a photomultiplier located to receive light from said filter.

117. The apparatus of claim 116, wherein a computer is coupled to the photomultiplier, for analyzing the output of the photomultiplier to assign relative fragment lengths and colors.